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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,672	12/21/2005	Ian W. Rodger	21411P	1366

210 7590 11/10/2009

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
11/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,672	RODGER ET AL.	
	Examiner	Art Unit	
	JENNIFER M. KIM	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-14 and 16-20* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-9, 14 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed September 9, 2009 have been received and entered into the application.

Action Summary

The rejection of claims 1-3 and 5-8 under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. (J Clin Pharmacol., 2001) is being **maintained** for the reasons stated in the previous Office Action.

The rejection of claims 9, 14 and 20 under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. (J Clin Pharmacol., 2001) as applied to claims 1-3 and 5-8 above, and further in view of Merck & Co, Inc. (1998) (MERCK) and Physicians' Desk Reference, 53 Edition, 1999 (PDR) is being **maintained** for the reasons stated in the previous Office Action.

Response to Arguments

Applicants' arguments filed September 9, 2009 have been fully considered but they are not persuasive. Applicants argue that Schwartz et al. does not described reducing the patients' total exposure to the DMARD because their dosage of methotrexate were maintained during the entire 3-week study. Applicants further

argues that the claim 1 has been amended to recites: "A DMARD sparing method for treating a chronic inflammatory disease or condition in a human patient in need thereof, comprising administering to the patient a therapeutically effective amount of a DMARD in accordance with a DMARD dosage regimen for a period of time, and thereafter: co-administering to the patient a therapeutically effective amount of a DMARD and a cyclooxygenase-2 selective inhibitor in accordance with a combination dosage regimen, ***whereby the total exposure to the DMARD is" reduced***" (emphasis added). This is not found to be persuasive because the claimed mechanism of action that the total exposure to the DMARD is reduced is inherent property of the same method step comprising administration of the same active agents with the same dosage amount to treat the same disclosed population as taught by Schwarz et al. That applicants may have determined a mechanism by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel or even unobvious the treatment of the conditions encompassed by the claims. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. (J Clin Pharmacol., 2001).

Schwartz et al. teach that a randomized double-blind, placebo-controlled study in rheumatoid arthritis patients on stable dosages of methotrexate. Schwartz et al. teach the patients were treated with 7.5mg to 20mg weekly of methotrexate for at least 1 month prior to the study. Schwartz et al. teach that the during the entire 3-week study, the patients maintained their regularly prescribed weekly dose of oral methotrexate, individualized by each patient's prescribing physician. Patients received their weekly oral dose of methotrexate (7.5mg to 20mg) (mean $\pm$ SD dose of methotrexate = 13.9 $\pm$ 4.0mg) on days-1, 7, 14 and 21. After the initial dose of methotrexate on (day-1), patients were randomly assigned to received rofecoxib 12.5mg, 25mg or 50mg during days 1 to 7, 8 to 14, and 15-21, respectively, in a step wise, ascending-dose sequence, or they were given matching placebo tablets on days 1 to 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9, 14 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. (J Clin Pharmacol., 2001) as applied to claims 1-3 and 5-8 above, and further in view of Merck & Co, Inc. (1998) (MERCK) and Physicians' Desk Reference, 53 Edition, 1999 (PDR).

The teachings of Schwartz et al. as applied as before. Additionally, Schwartz et al. teach that a dose-dependent increase in the plasma methotrexate AUC of approximately 23% and 40% was observed during concomitant administration with 75mg and 250mg once-daily rofecoxib, respectively. (page 1121, left-hand column).

Schwartz et al. do not teach the reducing the amount of methotrexate by 2.5mg per week set forth in claim 9, eliminating methotrexate (DMARD) and continuing therapy with rofecoxib set forth in claim 14, and further co-administering COX-2 inhibitor.

MERCK teaches that VIOXX (rofecoxib) 75mg coadministered daily for 10 days increased plasma concentrations by 23% as measured by AUC0-24 in patients receiving methotrexate (MTX) 7.5 to 15mg/week for rheumatoid arthritis. MERCK teaches that standard monitoring of MTX-related toxicity should be continued when VIOXX and MTX are administered concomitantly. (page 13, under Methotrexate).

PDR teaches that MTX is available in 2.5mg tablets. (page 1401, middle column under Oral).

It would have been obvious to one of ordinary skill in the art to modify the teaching of Schwartz et al. and to decrease the dosage of MTX by 2.5mg per week for those rheumatoid arthritis patients of Schwartz who are in need of 75mg rofecoxib. One would have been motivated to make such a modification because both MERCK and Schwartz teach that the plasma concentration of MTX increases when coadministered with 75mg rofecoxib. It is noted that the MTX is available in 2.5mg tablets as taught by PDR. One would have been motivated to decrease the dose of MTX by 2.5mg per week in order to avoid the MTX related toxicity for those patients in need of therapeutic

dosage of rofecoxib of 75mg with most safe and therapeutic amount of MTX. One of ordinary skill in the art would obviously continue to decrease the dosage of MTX per week in order to achieve the safe and effective rheumatoid arthritis therapy until the toxicity is eliminated.

Further, to continue treating Schwartz rheumatoid arthritis patients with rofecoxib, such is obvious choice of the attending clinician since rofecoxib is effective for the treatment of rheumatoid arthritis. The attending clinician would take account of the both pros and cons of administering rofecoxib, MTX or the combination and make optimum choice for the patients to be treated (e.g. patient previously suffer from MTX toxicity). Moreover, one of ordinary skill in the art would further combine COX-2 inhibitor in order to achieve an additive effect of obtaining anti-inflammatory effect of COX-2 inhibitors in the treatment of rheumatoid arthritis.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1617

Jmk
November 9, 2009